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ON THE USE
OF
IODIDE OF ETHYLE,

AND OTHER

O-CARBON COMPOUNDS,

IN

NARY CONSUMPTION.

BY

HENRY FISHER, M. D.



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ON THE USE
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I O D I D E O F E T H Y L E ,
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IN
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THE discovery of the anaesthetic properties of sulphuric ether and chloroform mark an important era in the history of medical science, both as regards the immense alleviation of human suffering due to their employment in surgical and obstetric practice, as also in leading to the investigation of the medicinal properties of similarly constituted bodies, and their employment in pulmonary disease. The radical ethyle, of which sulphuric ether and chloroform are compounds—the former as oxide and the latter as chloride—is composed of hydrogen and carbon only, and forms one of a series of similar radicals, differing only in the number of atoms of the constituent elements which enter into their composition. They all, or nearly all, possess anaesthetic properties, and are capable of forming compounds with other bodies used in medicine ; to their combinations with which they owe

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their value in the treatment of disease. The compounds of ethyle, methyle, and amyle, are those which have received the most complete investigation; but the ethyle series contains the best known, the most frequently used, and probably the most valuable of the hydro-carbon compounds. Their anaesthetic properties appear to depend entirely on the presence of carbon—the hydrogen playing an unimportant part in the production of unconsciousness, as is apparent from the development of similar phenomena by such substances as the chloride and sulphuret of carbon, into the composition of which hydrogen does not enter—while, on the other hand, we are not acquainted with any anaesthetic agent which does not contain carbon. It is not, however, to the production of anaesthesia by the ethyle compounds, but to the important part which they, in common with other hydro-carbon bodies, may be made to play in the treatment of phthisis pulmonalis, that I wish to direct attention. Uncombined ethyle has not, as yet, been used for medicinal purposes, nor is it probable that it will be so; its preparation is difficult and tedious; its properties can be only purely anaesthetic, and in all likelihood not more actively so than those of its well-known chloride.

Ethyle may be prepared by the decomposition of the vapor of its iodide, by the agency of metallic zinc, in a suitable apparatus, under considerable pressure; iodide of zinc is formed, and the ethyle makes its appearance as a mobile liquid, along with two other substances, which are at the same time spontaneously produced, namely, olefiant gas and hydride of ethyle. As these two substances are only compressed, and not liquefied, they are

evolved first on opening the apparatus; after a few moments the liquid ethyle begins to boil, and separate in the gaseous form, and as soon as a sufficient amount has been volatilized to obliterate the least traces of the other two bodies, may be collected over mercury. Ethyle thus obtained is a colorless gas, of a specific gravity of 2; it is not condensed at 64° F., the ordinary temperature of the atmosphere, but is liquefied 37° 5' Fahrenheit by a pressure of two and a half atmospheres; the boiling point is probably as low as 73° 4' Fahrenheit. In its deportment with other substances, it exhibits the same indifference which is observed with hydrogen at the common temperatures, and it is unaffected by sulphuric, nitric, or chromic acids. Hitherto chemists have not succeeded in reproducing from ethyle any of the numerous substances in which its existence is pre-supposed; but as a step in this direction has been recently taken, by the reproduction of alcohol from olefiant gas, it is a result which, in the present progressive state of the science of organic chemistry, may be justly anticipated. Ether and chloroform, the oxide and chloride of ethyle, are the first-discovered anaesthetics, and are among the number of substances which, from their volatility, have suggested their application to the treatment of pulmonary disease by inhalation, and in this way they have been found of considerable advantage in allaying bronchial irritation, appeasing cough, and rendering expectoration more easy; but their highly anaesthetic properties, and the impossibility of uniting them with substances possessing a direct local curative action, or with such as influence the con-

stitution generally, form an objection to their use in the treatment of consumption.

The above-mentioned indications of producing a local sedative and curative action, joined with the constitutional alterative and tonic action of an esteemed remedy, such as iodine, are admirably fulfilled by the employment of iodide of ethyle—by far the most valuable and important of the volatile hydro-carbons I shall have occasion to mention. Iodine has been used as much as any other substance for inhalation in consumption, but its irritating properties render it unfit for direct application to so delicate an organ as the lung, and, in consequence, it had for this purpose been almost entirely laid aside, until it was suggested by Dr. Turnbull, of Liverpool, that it should be given along with a compound possessing the necessary degree of volatility, as well as one which would disarm and nullify its irritative action. That desideratum is fulfilled by its employment in chemical combination with ethyle, and that the public and profession are largely indebted to Dr. Turnbull for its introduction to use will, I think, be admitted by all who have given the remedy a trial.

The *iodide of ethyle* is a volatile, transparent, colorless fluid, having a specific gravity of 1920; its boiling point is 130° Fahrenheit; it is sparingly soluble in water, and has a taste and odor somewhat resembling chloroform, which it also imitates in its anaesthetic action, although in this respect it is a much less active agent. Formulae for its preparation are given in all the recent works on organic chemistry, and may be easily followed by any one accustomed to chemical manipulation. Care must be taken that it does not become contaminated with

any of the phosphorus used in its production, and the absence of this substance must be determined, before its employment, by the application of the usual tests. The purity of the substance being ascertained, there is none which can be more safely or easily used by way of inhalation. It exhibits the usual sensitiveness of the iodides to the action of light, and is apt to become discolored, owing to the liberation of a little of the iodine—a circumstance which does not affect the purity, although it slightly impairs the strength of the preparation.* Iodide of ethyle has been given internally, in doses of from five to twelve minims, in many cases where iodine would have been an appropriate remedy; it acts as a stimulating and alterative tonic, often improving the appetite and general health; its odor may almost always be perceived in the breath of those who have taken it for a few days, the same being the case with those taking oxide of ethyle, whilst no such effect is produced by the preparations of methyle, from which circumstance it has been argued that there is a special tendency to the elimination of the ethyle compounds through the lungs. The dose for inhalation may vary from five to thirty minims; it may be simply dropped on a handkerchief, and so inhaled—and it is in this way that I have most frequently exhibited it—but I have reason to believe that an inhaling apparatus, which will provide for a due admixture of atmospheric air, may be advantageously employed. In order to show the action of the remedy, I may here re-

* Iodide of ethyle is manufactured in perfect purity by Messrs. A. Cushman & Co., 295 Broadway.

capitulate the history of four cases, briefly reported by me in a recent number of the New York Medical Times. The first is that of H. P., a young man, age 19, who commenced the use of ethyle on the 1st December, 1854, at which time he presented the following symptoms: had suffered from cough for eight months, the cough being attended, latterly, with muco-purulent expectoration; the sputa were frequently streaked with blood, and once about half an ounce of what was described as being unmixed arterial blood was raised; there was some dyspncea, and considerable pleuro-dynic pain after exercise; nocturnal hectic was of tolerably frequent occurrence; and there was general lassitude and debility. There was marked dullness anteriorly on the right side of the thorax, extending from the second to the fourth intercostal spaces, where also there was obscuration or obliteration of the natural respiratory murmur; moist mucous rale and ronchus were audible, and there was pretty distinct bronchophony. In other portions of the right side, and over the left side of the thorax, the respiration was exaggerated and puerile, but otherwise presented no indication of disease. He had taken cod-liver oil, and employed counter-irritation over the affected lung without much amelioration of the thoracic symptoms, but he had gained somewhat in weight. He now commenced inhaling the iodide of ethyle, using fifteen minims three times a day, and continued it regularly for more than two months, when it became necessary to suspend its use, owing to diarrhea, frontal head-ache, and other symptoms of iodism having made their appearance. Previous to these symptoms, and after their subsidence, which took place shortly

on the suspension of the remedy, his condition was and has been most satisfactory ; he has scarcely ever coughed ; there has been no return of hectic or hæmoptysis ; and he has been gaining flesh and strength rapidly. The chest, on percussion over the affected portion, indicates but very slight dullness, and the respiratory murmur approaches very nearly a natural character.

In another case, which presented the symptoms of tubercle in its earliest stage, accompanied with severe bronchitis, the use of the ethyle for a few days, combined with counter irritation, confinement, and a strict antiphlogistic regimen, sufficed to effect a complete suppression of the cough and dyspnœa, which, as yet, after an interval of some months, have not re-appeared.

Other two cases, in which I have had an opportunity of testing its utility with regularity, presented unmistakable evidence of the existence of a small cavity—in the one case occupying the right, in the other the left, lung. In both these cases the severity of the symptoms has been much mitigated, and the progress of the disease arrested ; and I believe it to be possible that a cicatrizing process may be yet established.

Since the above cases were reported, the hopes then entertained have, to a considerable extent, been confirmed. Both of those last mentioned, have progressed most satisfactorily, and have been enabled to resume active out-of-door employments. Out of many others, in which I have had an opportunity of employing the remedy in various stages of the disease, several have been much benefited by it. The tonic and stimulant action of the iodine is established, cough, dyspnœa, and

bronchial irritation generally, relieved, and the quantity of the expectoration diminished. The trials, so far, go to prove that the theoretical conclusions to be drawn from a consideration of the chemical nature of the substance were correct, and that it will be a most valuable addition to our means of treating consumption. Firstly, by its exerting a direct sedative and local curative action on the diseased part, and secondly, from absorption, a general and constitutional action ; and, in these ways, it will exert an influence in the earlier stage of tubercular disease, by promoting absorption, and later, by aiding cicatrization.

The circumstances to be guarded against, in its administration, are, the production of anaesthesia or the development of iodism. The small doses I have recommended have it scarcely in their power to produce unconsciousness, and when the tolerance of a certain amount has been once established, it may be repeated with the utmost confidence. The production of iodism will be attended with the usual premonitory symptoms, but as their appearance is neither necessary or desirable, it will be judicious to intermit the exhibition of the remedy, at stated intervals, for some days. The urinary secretion ought, also, during a course, to be frequently examined, and the readiness, or otherwise, with which the usual tests indicate the presence of iodine, will form a guide as to the advisability of a diminution or suspension of the dose prescribed. It is worthy of remark that soon after the use of the remedy has been commenced, the presence of iodine in the urine can be readily shown by means of the starch and acid test, and as the iodide

of ethyle itself, is insensible to the action of this test, it is obvious that it must be decomposed in the system, the ethyle being probably eliminated through the lungs, the iodine uniting with some of the substances with which it comes in contact. If it is wished to demonstrate the presence of iodine in the iodide of ethyle, this can be readily done in the usual way with oxide of manganese and sulphuric acid.

The expensive nature of the substance, and the difficulty of procuring it in sufficient purity, form at present a serious barrier to its employment, and have induced some, as I have elsewhere mentioned, to use in its stead a mechanical solution of iodine in sulphuric ether. If the employment of this mixture is attended with any benefit, it must be owing entirely to the sedative action of the ether, as very little, if any, of the iodine, will become volatilized—a fact of which any one may easily convince himself by placing a portion of the solution in a watch-glass evaporating dish, or other suitable vessel, previously weighed, permitting evaporation to take place, when the side of the vessel will be coated with iodine, and it will be found to have gained in weight in exact proportion to the quantity previously held in solution by the ether.

While advocating the claims of iodide of ethyle upon the attention of the profession, I would not have it supposed that I recommend it as a substitute for other and better-known remedies, or for the strict enforcement of the hygienic and dietetic rules which form the most valuable part of what may be called the routine treatment of phthisis; but to these, I believe, it will be found

a most valuable adjunct. I do not doubt that the real and primary cause of the disease is to be sought for in defective action of the organs of assimilation, and also that its ultimate cure, if ever, is to be found in the restoration of the healthy discharge of these functions, and that it is to the attainment of this object that our efforts should be mainly directed. This must, of necessity, be a work of time, and I believe that the iodide of ethyle, while aiding the measures which we employ for this purpose, by its general alterative and tonic action, is also, by its local effect on the diseased part, gaining us time for the full development of our plans.

The *acetate of ethyle*, the next of the volatile hydro-carbon compounds I shall speak of, has been found to possess considerable anæsthetic properties: it has been given internally as a diffusible stimulant and as a remedy in some forms of pulmonary disease; its action appears to be exerted on the bronchial mucous membrane; and it has been found to relieve difficulty of breathing, cough, and bronchial irritation in many cases of consumption and bronchitis; but its most important property is its astringent action upon the mucous surface, and in cases of excessive secretion, it has been found to have a very decided power in checking the quantity of expectoration. Most medical men dread the use of astringents in chronic bronchitis, and rather exert their efforts to promote expectoration, under the belief that a contrary course would lead to an increase

- of the sense of tightness and difficulty of breathing; but experiments with the acetate of ethyle go to prove that this is not always the case; that benefit may be derived

from their use, by imparting tone to the bronchial mucous membrane; and it is urged that to use them in chronic inflammations of this tissue, is as reasonable as to apply astringent remedies to act specially on the lining membrane of the bowels or bladder when similarly affected.

Methyle is the base of wood spirit, which is the hydrated oxide of methyle. Its acetate and iodide are possessed of properties somewhat similar to the analogous compounds with ethyle. The acetate is a thin ethereal fluid, with an odor like naphtha, and, like this substance, has considerable value as a means of checking excessive vomiting; but its principal use is in the power which it possesses of checking excessive secretion from the bronchial mucous membrane, and for this purpose it has been used with success in cases of chronic bronchitis. Iodide of methyle is a transparent, oily-looking fluid, having the odor of wood spirit, sparingly soluble in water, very heavy, its specific gravity being 2257. It acts, like similar compounds, as a powerful diffusible stimulant, and produces, also, the physiological effects of iodine. The anaesthetic properties of the methyle compounds are not well marked, and their properties are so pungent and irritating as to render them objectionable for general use.

The acetate and iodide of amyle have met with but few trials: they have nothing to recommend them in preference to the ethyle compounds, and like those of methyle, are harsh and irritating to a degree which will probably preclude their employment.

The iodides of all the three bases mentioned, unite

readily with lard, and have been used in this form as local applications to chronic, indolent, scrofulous and irritable ulcerations of the surface. The iodide of amyle produces much heat and smarting, and is, therefore, objectionable, but both the other compounds have been used with advantage of a very marked nature, for ulcerations, more especially those of a scrofulous nature, the iodide of ethyle being particularly beneficial for painful or irritable ulcers, as it produces an anodyne effect, and does not cause so much smarting as the other more stimulating applications. The effect of these substances upon superficial ulcerations, is interesting, as bearing upon the hopes entertained of a cicatrizing process being promoted by the application of their vapor to similar lesions of the pulmonary tissues.

The *bromide of ethyle* is a substance which may probably be found of use: it has an agreeable aromatic odor and taste; it is stated to be of low anaesthetic power, and to have properties in other respects resembling the iodide, but is more difficult of preparation.

Another hydro-carbon compound alcohol, or the *hydrated oxide of ethyle*, has frequently played an important part in the treatment of consumption, and has led to results which might entitle it to a place among the many vaunted cures of the present day. I am not aware that it has ever been applied by means of inhalation; but that its copious use in the usual way has led to recovery in cases which have been declared hopeless, every medical man in the habit of treating the disease can bear testimony. I have before me the report of a case which had all the symptoms of confirmed phthisis, from which

the patient recovered solely from the immoderate use of beer. He had engaged himself as a pot-boy, and had, in that situation, drunk almost *ad libitum*. It should be stated that the improvement had begun under the use of cod-liver oil, at the Brompton Hospital, but it had continued and even progressed more rapidly after it was left off. There is another case, so strikingly illustrative of the occasional effects of alcohol in this disease, reported in the lectures of Dr. Stokes, of Dublin, that I am tempted to give it in his own words. He says: "Some years ago I saw a gentleman who came to town, laboring under all the symptoms of well-marked phthisis. The disease had been of some months' standing, and the patient was a perfect picture of consumption. He had a rapid pulse, hectic sweating, purulent expectoration, and all the usual physical signs of tubercular deposit, and of a cavity under the right clavicle. I may also state that the history of the disease was in accordance, in all particulars, with this opinion. I saw this patient in consultation with a gentleman of the highest station in the profession, and we both agreed that there was nothing to be done. This opinion was communicated to the patient's friends, and he was advised to return to the country. In about eight months afterwards, a tall and healthy-looking man, weighing at least twelve stone, entered my study with a very comical expression of countenance:—' You don't know me Doctor,' he said. I apologized, pleading an inaptitude for recollecting faces. 'I am,' he said, 'the person you sent home to die last year. I am quite well, and I thought I would come and show myself to you.' I examined him with great

interest, and found that every sign of disease had disappeared, except that there was a slight flattening under the clavicle. Tell me, said I, what you have been doing? 'Oh,' he replied, 'I found out from the mistress what your opinion was, and I thought as I was to die, I might as well enjoy myself while I lasted, and so I just went back to my old ways.' What was your system of living? said I. 'Nothing particular,' he said; 'I just took whatever was going.' Did you take wine? 'Not a drop,' he replied; 'but I had my glass of punch as usual.' Did you ever take more than one tumbler? 'Indeed I often did.' How many? 'Three or four? Ay, and more than that: I seldom went to bed under seven.' What was your exercise? 'Shooting,' he said, 'every day that I could go out.' And what kind of shooting? 'Oh, I would not give you a farthing for any but the one.' What is that? 'Duck shooting.' But you must have often wetted your feet? 'I was not very particular about the feet,' said he, 'for I had to stand up to my hips in the Shannon, for four or five hours of a winter's day, following the birds.' "

Many of the good results in this case are to be attributed to the general tonic and undepressing treatment to which the patient subjected himself, but at the same time this and similar cases are significant, as showing the advantage to be derived from a plentiful supply to the system, of a pure hydro-carbon compound, an hypothesis which the comparative immunity of the intemperate from phthisis appears to favor.

These facts are worthy of being borne in mind, in considering the action of the next hydro-carbon body I

shall treat of, namely, cod-liver oil, the ultimate analysis of which shows it to be composed principally of hydrogen and carbon, oxygen being present in small quantities, as also iodine, bromine, and traces of other substances.

Cod-liver oil has met with more success, has been more largely used, and has attained a greater reputation than any other remedy employed in the treatment of consumption ; its good effects are almost universally admitted, while its mode of action still holds open an interesting field for inquiry ; an investigation which, I believe, will be facilitated by a brief review of the state of system which this remedy is intended to obviate. That phthisis is intimately connected with dyspepsia, is no new theory. Abernethy in his great work has drawn attention to the laws under which many so-called local diseases proceed from constitutional causes. Previous to this time (1823), consumption had been generally considered to be a disease of the lungs only ; and although it was known to be hereditary, and peculiarly apt to occur in certain temperaments, yet in the list of its causes we meet with very slight mention of those involving the idea of depraved nutrition. Dr. Philip, who writes about the same time, boldly places phthisis as the third stage of dyspepsia, and devotes much excellent observation to the symptoms and treatment of the phthisical form of the latter. He fails, however, to make his generalization sufficiently comprehensive to grasp the whole truth, and states only that some forms of indigestion end in phthisis, not that all or almost all phthisis begins in indigestion. Lepelletier, in his trea-

tise on scrofulous diseases, makes a strong and clear statement as to the connection of struma with disease of the nutritive system. He arranges its causes under three heads : those which impair the assimilating action, those which present insufficient elements of nutrition, and those which impede excretion. Ayre and Marshall Hall have shown prominently, the cachexia accompanying tubercular disease. Dr. Todd, in his article on indigestion, in the Cyclopædia of Practical Medicine, describes a strumous dyspepsia, and insists on its constant presence in the scrofulous habit. Dr. Bennett, in his work on Pulmonary Tuberculosis, remarks that, from facts of a certain kind, it has been supposed that hereditary predisposition, a vitiated atmosphere, changeable temperature, certain occupations, humidity, particular localities, and so on, predispose to phthisis. Very frequently, several of these are found united, so that it is difficult to ascertain the action of each ; but when they so operate, they invariably produce in the first place more or less disorder of the nutritive functions, and are associated with dyspepsia or other signs of mal-assimilation of food. Recent researches, especially those of Hutchinson, have shown that if the history of a given number of cases of phthisis be examined, it will be found that a large majority have had a well-marked-dyspeptic seizure of longer or shorter duration, previous to the appearance of the tubercular symptoms ; and he has shown, with much ingenuity, that this dyspepsia, which precedes and accompanies the disease, is characterized by an inability to assimilate the hydro-carbonaceous substances, this inability probably

depending on defective or faulty secretion of the biliary and pancreatic fluids.

The circumstances which lead to this conclusion, are the establishment of the fact, that in the dyspepsia which precedes or accompanies a majority of the cases of phthisis, the earliest and most prominent symptoms of a very large proportion, is a dislike of fat, in many cases amounting to extreme aversion ; that this distaste for fatty substances is accompanied by an inability to digest them, when swallowed, as is shown by the occurrence of pyrosis, flatulency, nausea, head-ache, and other symptoms of indigestion ; that the dislike, in severe cases, extends to other hydro-carbonaceous substances ; and that exactly coincident with symptoms indicative of an inability to digest the hydro-carbons, there usually occurs another, namely, emaciation. The connection between the two is plain. The blood being no longer supplied by the digestive organs with its due quantity of fuel pabulum, the re-absorption of the adipose tissue of the body takes place to supply its want. The fat disappears from the sub-cutaneous tissue, the patient loses weight, and is observed to be thinner. If phthisical dyscrasia advance, the whole available adipose tissue is soon used up; and now commences the attack of the hyper-oxygenated blood on the other tissues of the body ; the muscles, the cellular tissue, and the skin become thinned down by interstitial absorption, until the patient is reduced to the skeleton-like constitution by which the terms phthisis and consumption have been originally suggested. The treatment of this form of dyspepsia, whether preceding or associated with phthisis, is obvious ; it is, of course, impossible to

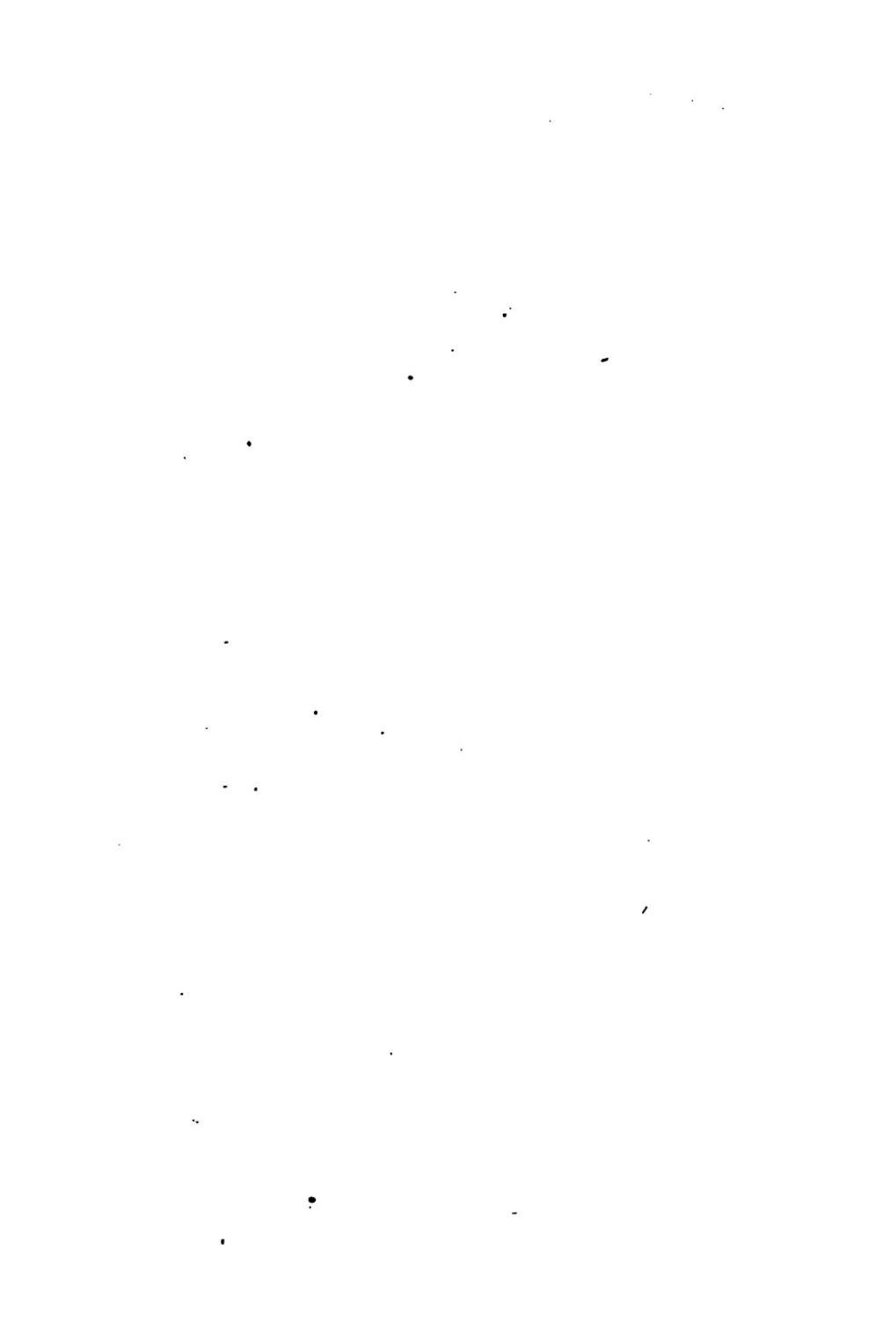
order the use of fat to the subject of it: in the first place, his palate would refuse it; in the second, if swallowed, his stomach, pancreas, and liver are quite incompetent to its digestion. It is not, however, by any means so with cod-liver oil. Whether it be that the biliary principles which it contains furnish the necessary materials for the assimilation of the oily ones, or whether these biliary principles, or the minute quantities of iodine, bromine, or phosphorus present, exert a beneficial influence on the viscera at fault, and excite their latent functions, cannot be positively determined; but the fact is nevertheless certain, that the oil can be endured by the subjects of the most aggravated dyspepsia, and will relieve symptoms which all *a priori* reasoning would have expected it to aggravate. The rule, then, should be, in all cases of phthisis, to give the oil a trial; and when, by use, it has come not only to be tolerated, but liked, and the relish for the hydro-carbons has been restored, to supply them. Butter, cream, milk, eggs, sugar, dried fruits, and even fat bacon and pork—also the moderate use of alcohol, in its various forms—should be recommended; and the usual rules with regard to exercise, bathing, &c., strictly enforced. Cases will, of course, occur in which the oil will not be borne, but in some this complication may be overcome by judicious treatment; and the difficulty of the assimilation of fatty matters, there is reason to believe, may be made use of for the purposes of prognosis, for it is assumed that the severity of the tubercular dyscrasia may be measured by the difficulty with which the cod-liver oil is borne. Great discrimination and care are requisite in the selection of

remedies to assist the stomach in the digestion of the oil. The substances used are exceedingly various; some cases are benefited by the vegetable bitters, more especially calumba; others by the use of bismuth, or the mineral acids, while not a few improve under the use of mercury in very minute doses. But it is impossible to lay down general rules for the employment of these substances: their application must vary with the merits of each individual case.

The recent employment of *oleine*, prepared from cod-liver oil, bids fair to do away with many of the objections which have hitherto attended its use. The process employed consists in subjecting the oil to considerable pressure at a very low temperature, by which means the oleine is separated from the stearine and margarine. Oleine thus obtained is a very liquid, and, at ordinary temperatures, a very transparent fluid, agreeing in color with the oil from which it is prepared; the ordinary yield is about seventy-five per cent. The active principles of cod-liver oil are retained in the oleine, while those which are merely excrementitious are got rid of in the separation of the margarine and stearine. The oleine has been given with success in cases in which the administration of the oil had been attended with severe nausea and vomiting; and experiments instituted with the margarine and stearine show that they are capable of producing symptoms exactly similar to those caused by the oil itself, before being freed from them; from which circumstances it may be presumed that, in the oleine, we have the means of extending the benefits of this useful remedy to

a class of cases in which previously its exhibition could not be persisted in.

In the preceding paper I have endeavored to call attention to a very useful class of remedies, and to a view of the nature of consumption, which is in accordance with the results to be sought for in their employment. I shall be satisfied if my remarks lead to a more extended trial of the substances spoken of, or if they in any way tend to dispel the delusion that phthisis is a localized disease of the lung, and its cure to be sought in topical applications only.

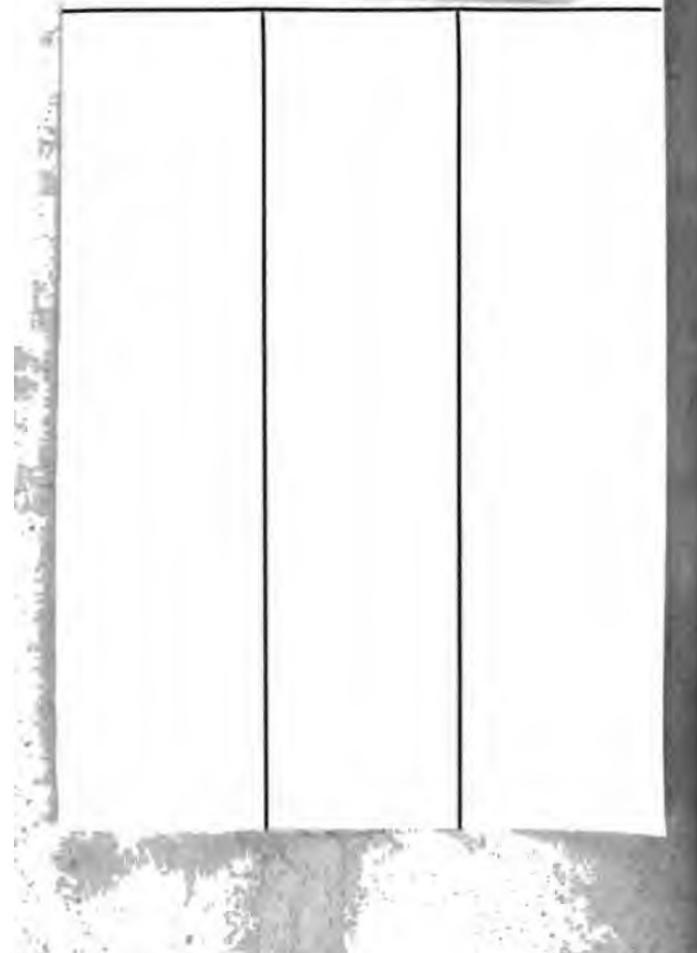






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